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First and second law work production efficiency of a muscle cell

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ABSTRACT

The absolute value of the muscle efficiency and its decrease over time has vital consequences. Among other diseases heart failure, which is the leading cause of death in developed countries is dramatically affected by muscle weakness. This paper provides an analogy between the Carnot engine and muscle to gain insight on the muscle work production process and estimate the maximum muscle efficiency under physiological conditions. An "ideal muscle" model, which operates steadily and reversibly, is defined and for this model energy and exergy analyses are performed. Theoretical results are compared with the experimental measurements.

Key words: metabolism, muscle work, thermodynamic efficiency, first law, second law

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Nomenclature

B	Stream availability	kJ/kmol
E	Total energy	kJ
F	Force applied to a muscle or exerted by the muscle in an elongation experiment	N
h	Enthalpy	kJ/kmol
I	Ionic strength	mol
m	Mass	kg
P	Pressure	N/m^2
Q	Heat	kJ
s	Entropy	kJ/(kmol K)
T	Temperature	K
W	Work	kJ
X	Exergy	kJ
η	Efficiency	Fraction or percentage
μ	Chemical potential	kJ/kmol
Subscripts		
0	Restricted dead state	
I	First law (energy)	
II	Second law (exergy)	
blood	Pertinent to blood	
i	Any species	
in	Inlet	
k	Index of heat sources	
muscle	Pertinent to muscle	
out	Outlet	
R	Reaction	

1. Introduction

Muscle work efficiency is a topic of interest to muscle physiologists and has been explored by relatively few experimentalists (Gibbs and Chapman 1974; Heglund and Cavagna 1987; Barclay 1996, 2008, 2012; Barclay and Weber 2004; Smith et al 2008). Efficiency of conversion of chemical energy into work in muscles is not constant. On the contrary, it may change substantially depending on the physiological conditions. The decline of the muscle efficiency has vital consequences, such as heart failure (Mariunas *et al* 2008; Ribeiro *et al* 2012; Barclay 2008). About 600,000 people die of a heart disease only in the United States every year (Murphy et al 2013). Decrease of the muscle efficiency, which may also be expressed as the "*muscle weakness*" occurs in 30 to 50% of the heart failure patients (Ribeiro et al 2012). People lose approximately 20 to 30% of their muscles between the ages of 20 and 80 (Kiriazis and Gibbs 2000, Carmeli et al 2002); the age related loss of muscles is related with the mitochondrial functioning and the cellular energetics and accompanied with the loss of the efficiency (Carmeli *et al* 2002). The decrease of muscle efficiency is also among the causes of the fatigue (Mariunas et al 2008). Estimating the theoretical maximum muscle efficiency may help us to assess a patient's actual muscle performance, the degree of muscle loss and how close they are to experience a heart problem, if the in vivo muscle efficiency can be determined via appropriate measurements.

The theoretical maximum muscle efficiency can be determined by performing an energy and an exergy analysis. The energy (or first law) efficiency of a muscle is calculated as the ratio of the work done to the energy utilized to achieve it. A fraction of the utilized energy may actually not be converted into useful work, but utilized to overcome the associated unavoidable difficulties, such as friction or other irreversibilities (Struchtruo and Rosen 2002). The exergy efficiency is calculated as the ratio of the work done to the exergy utilized to achieve it. Exergy is not a conserved property; it is destroyed due to irreversibilities (Szargut *et al.* 1988, Szargut 2005). Exergy destruction may be reduced by changing the path of a process; therefore, exergy analysis provides useful information via pointing the losses and enables researchers to analyze an existing process and find new paths to avoid losses (Ayres 1998, 1999; Caton 2000; Rakopoulos and Giakoumis 2006; Talens *et al* 2007; Petela 2010; Sorgüven and Özilgen 2010, 2012). Exergy analysis of biological processes is a relatively new subject. There are limited applications for cellular processes (Silva and Annamalai, 2008; Ketzer and de Meis, 2008; Lems *et al* 2009; The and Lutz, 2011; Mady *et al* 2012; Mady and de Olivera Jr., 2013; Genç et al., 2013a; Sorgüven and Özilgen, 2013).

This paper is organized as follows: First, an "ideal muscle", which involves no internal irreversibilities, is defined. Then, this model is employed to calculate the theoretical limits for the muscle efficiency. Last section compares theoretical results with the empirical measurements.

2. "Ideal Muscle" Model

Main purpose of a muscle cell is to perform mechanical work for motility in form of walking, running, swimming and flying. To produce work, muscle cells catabolize nutrients. Glucose is the mostly favored nutrient in the energy metabolism. Glycolytic pathway essentially breaks glucose into carbon dioxide and water:

$$Glu + 6O_2 \rightarrow 6CO_2 + 6H_2O \quad (1)$$

A part of the energy released by this reaction is dissipated as heat and the rest is used to synthesize adenesine tri phoshate (ATP) (Eqn. 2). Depending on the physiological conditions, glycolytic pathway produces 30 to 38 moles of ATP (Lehninger, 1982).

$$ADP + P_i \rightarrow ATP \quad (2)$$

ATP is hydrolyzed to adenesine di phosphate (ADP) and inorganic phosphate (P_i) in muscle cells to contract muscle fibers and perform mechanical work (Eqn. 3).

$$ATP \rightarrow ADP + P_i \quad (3)$$

The “ideal muscle” is defined as a reversible work producing system analog to a Carnot heat engine (Fig. 1 and 2). In a biological system operating at constant temperature heat can never be converted into work; therefore, the biological systems actually work on totally different principles than the heat engines. Wilkie (1960) and Woledge *et al* (1985) have noted that it would be misleading to compare muscle to a heat engine. In this study muscle is not compared to a heat engine, but an analogy is established between them. An analogy model may be suggested to make it possible to develop a mathematical model for a little known process by considering its similarity with a well-known process (Özilgen 2011). Carnot engine is a highly useful concept employed in engineering thermodynamics. Studies regarding the thermodynamic aspects of the muscle work are much limited in scope, when compared to those related with the heat engines; therefore, establishing an

analogy between these systems may help us to understand the thermodynamic aspects of the muscle work better by benefiting from the concepts regarding the thermodynamic aspects of the Carnot engine.

Carnot heat engine takes heat from a high thermal reservoir and produces work. Analog to that, the ideal muscle takes Gibbs free energy of nutrients and O_2 from a high chemical potential reservoir, and produces work. Table 1 lists the analog components of the Carnot engine and the ideal muscle. The ideal muscle is in contact with an artery, which has a high concentration of nutrients and O_2 (i.e. high chemical potential), and a vein, which has a low concentration of nutrients and O_2 (i.e. low chemical potential) (Fig. 2). Blood is considered an ideal solution containing glucose, oxygen, carbon dioxide and water among other chemicals. Concentrations of chemicals in the blood are taken from previous studies (Genç *et al* 2011; 2013a, b). There are semi-permeable membranes between the reservoirs and the cell, which allow only nutrient and oxygen flow from the high potential reservoir, and only CO_2 and water flow to the low potential reservoir. We assume that the entire inflowing nutrient is converted into CO_2 and H_2O, and there are no side reactions and by-products. During the oxidation of glucose, 30 to 38 moles of ATP are produced. The ATP production reactions are considered reversible, which is a valid assumption, since the cellular biochemical reactions have efficiencies higher than 99% (Genç *et al* 2013a). The produced ATP is consumed to reposition the muscle fibers and contract the muscle. During muscle contraction ATP is hydrolyzed and ADP is produced (eqn. 3).

The model considers uniform temperature (T), pressure (P) and concentration (c) distributions throughout the system, where all heat and mass transfers occur between the cell and blood isothermally.

Differential change of mass, *m*, energy, *E*, and exergy, *X*, in the ideal muscle can be represented as:

$$\frac{dm}{dt} = \sum (\dot{m})_{in} - \sum (\dot{m})_{out} \quad (3)$$

$$\frac{dE}{dt} = \sum (\dot{m}h)_{in} - \sum (\dot{m}h)_{out} + \dot{Q} - \dot{W} \quad (4)$$

$$\frac{dX}{dt} = \sum (\dot{m}b)_{in} - \sum (\dot{m}b)_{out} + \dot{Q}\left(1 - \frac{T_0}{T}\right) - \dot{W} + P_0 \frac{dV}{dt} - \dot{X}_{loss} \quad (5)$$

Where P_0 is the restricted dead state pressure and *b* is the flow availability of a stream (neglecting the kinetic and potential energy contribution):

$$b = h - T_0 s - \sum x_i \mu_i^0 \quad (6)$$

Where μ_i^0 is the chemical potential of the pure species *i*. Numerical simulation of the energy metabolism shows that sudden changes in the metabolic conditions, such as a sudden decrease in blood glucose level or oxygen concentration, cause short-term instabilities and then the system reaches a new steady state within minutes after the disturbance (Genç *et al* 2013b). In the following analysis, we assume that the cellular conditions remain steady and hence, that the processes occurring in the ideal muscle are steady. All processes occur isothermally. If the thermal dead state for the exergy analysis is chosen as the cell temperature (T_0=T), then the exergy transfer due to heat becomes zero, implying that $\dot{Q}\left(1 - \frac{T_0}{T}\right) = 0$. Assuming that the surroundings work P_0dV is also zero, equations (3) - (5) can be rewritten as:

$$0 = \sum (\dot{m})_{in} - \sum (\dot{m})_{out} \quad (7)$$

$$0 = \sum (\dot{m}h)_{in} - \sum (\dot{m}h)_{out} + \dot{Q} - \dot{W} \quad (8)$$

$$0 = \sum (\dot{m}b)_{in} - \sum (\dot{m}b)_{out} - \dot{W} - \dot{X}_{loss} \qquad (9)$$

The significance of the terms employed in these equations are visualized in Figure 3, where it is shown that the difference between the in-flowing and out-flowing chemical exergy is equal to the sum of the work and exergy loss. When $\dot{X}_{loss} = 0$, then work produced achieves its maximum value. Equation 8 shows that if the muscle performs the maximum attainable work, W_{max}, then heat generation should be minimum, Q_{min}.

3. Discussion

We will employ the model to calculate the thermodynamic efficiency of the model under two different cases: (1) Theoretical limit of the maximum work production and minimum heat production in a muscle in a reversible process, (2) Theoretical limit of maximum heat production when no work is done. Then we will compare these limits with the minimum and the maximum measured heat releases (Table 3).

3.1. Theoretical limit of the maximum work production in a muscle in a reversible process

The term reversible implies that $\dot{X}_{loss} = 0$. Under these conditions the balance equations (8) and (9) yields:

$$\dot{W}_{\max} = \sum (\dot{m}b)_{in} - \sum (\dot{m}b)_{out} \qquad (10)$$

$$\dot{Q}_{\min} = \sum (\dot{m}h)_{out} - \sum (\dot{m}h)_{in} + \dot{W}_{\max} \qquad (11)$$

Equation (10) implies that $W_{\max}$ gets larger as the stream availability of the nutrients increase and the stream availability of the waste molecules decrease. Value of stream availabilities depend on the thermodynamic states of the reservoirs. If we assume that both reservoirs are at 310.15 K, pH=7 and I=0.18, and the metabolite concentrations are as given in (Genç *et al* 2013a), then the stream availabilities have the values listed in Table 2, and the maximum work and the corresponding heat release can be calculated as:

$$W_{\max} = \sum (mb)_{in} - \sum (mb)_{out} = 3862 \text{ kJ/mol glucose} \quad (13)$$

$$Q_{\min} = \sum (mh)_{out} - \sum (mh)_{in} + W = -4586 + 3862 = -724 \, kJ/mol \; glucose \quad (14)$$

The calculation, which is given here, is consistent with the procedure given by Constable *et al* (1997) who calculated the enthalpy output as the sum of the work done and heat released during contraction of a muscle. The estimates of the maximum and the maximum works of this study are consistent with the calculations of Smith *et al* (2008), as depicted in Table 3. Widen and Barclay (2006) suggested that the enthalpy output by the mouse papillary muscle was partitioned into force- dependent, and force independent fractions, pointing the importance of the unavoidable additional metabolic energy expense, accompanying the muscle work. The procedure described in this paper is different than that of Reggiani *et al* (1997), who based their calculations on the free energy change of the ATP hydrolysis, and experimentally determined mechanical work performance.

3.2. Theoretical limit of maximum heat production when no work is done

The maximum amount heat, which may be released from a muscle may be calculated as $Q_{max}=\Delta G + Q_{min}=4586$ kJ/mole glucose, which may be regarded as an important thermodynamical parameter, when we consider the inconsistent results of the experimental studies aiming to determine the thermic effects of the foods (Granata and Brandon, 2002). Curtin *et al* (2002) addressed this issue at the muscle level and partitioned heat production into heat due to contractile ATPases, and the recovery heat due to ATP supplying processes. Muscle enthalpy production and its relationship to actomyosin ATPase is described in detail by (Homsher 1987).

3.3. Comparison of the theoretical limits with the calculations based on the experimental data

The first law efficiency of the muscle work is defined in analogy with that of Carnot engine as:

$$\eta_I = \frac{W}{\Delta H} \qquad (15)$$

The maximum first law efficiency for glycolysis may be calculated after substituting W_{max} and $\Delta H = \Delta H_R$ in equation (15) as:

$$\eta_{I,rev} = \frac{3862}{4586} = 84\,\% \qquad (16)$$

The closest value to this calculation was reported by Jubrias *et al* (2008), who calculated that 68 % of the chemical energy available from ATP splitting was converted to external work output in human first dorsal interosseous muscle.

The second law efficiency is defined as the ratio of the actually produced work to the maximum available work:

$$\eta_{II} = \frac{W}{W_{\max}} = \frac{W}{\sum (m_j b_j)_{in} - \sum (m_j b_j)_{out}} = \frac{W}{\Delta G} \qquad (17)$$

Equation (15) implies that $W = \eta_I \Delta H$, therefore the second law efficiency can be rewritten as:

$$\eta_{II} = \eta_I \frac{\Delta H}{\Delta G} \qquad (18)$$

Equation (18) is consisted with the explanations of the experimentalists, who suggest that the development of the inefficiency is mainly caused by inefficient ATP (or substrate) use by ion pumping, which contributes to the denominator of the efficiency expression. The proponents of the idea suggest that the pools allow ΔG_{ATP} to be maintained at high values even in the face of considerable ATP turnover (Vendelin *et al* 2004; Barclay 2008; Joubert *et al* 2002 and 2008).

Theoretically determined values of η_I and η_{II} are compared with the calculations based on the experimental measurements in Table 3, and perfect agreement is observed. We see that the theoretical maximum work (W_{max} =3862 kJ/mol glucose) is larger than the maximum experimentally determined value (3707 kJ/mol glucose) as reported by Smith et al (2008). In the same analysis, the theoretically determined minimum heat is 724 kJ/mol glucose and it is lower than the corresponding experimentally determined value as reported by Smith et al (2008) as 879 kJ/mol glucose. The theoretical maximum η_I and η_{II} are calculated as 0.84 and 1, respectively. The experimentally n-measured maximum η_I and η_{II} are 0.81 and 0.96, respectively (Table 3). When we consider the second case, e.g., theoretical limits of the parameters with the maximum heat release and the minimum work performance, we again see an almost perfect agreement. While the theoretically determined W_{min} =0 kJ/mol glucose, its experimentally determined counterpart was 569 kJ/mol glucose, and the theoretically determined maximum heat release was 4586 kJ/mol glucose, while its counterpart based on the experimental data was 4017 kJ/mol glucose; theoretically determined η_I and η_{II} are both 0, whereas their counterparts based on the experimentally determined data are 0.12 and 0.14, respectively and imply an almost perfect agreement between the theoretical and experimental cases.

Numerous experimental and analytical studies are performed to determine the heat released and work produced via muscle contractions since the pioneer work of Hill (Reggiani *et al* 1997; Holmes, 2006). Energy (either enthalpy or free energy), which is released upon ATP hydrolysis depends on cellular conditions (Alberty 1969; Woledge and Reilly 1988). For example, determinations of standard free energy of ATP hydrolysis are made at specified pH, ionic strength and temperature and calculation of actual ΔG_{ATP} takes account of

concentrations of ATP, P_i and ADP. This observation is consistent with the model suggested by Genç *et al* (2013a), where the Gibbs free energy and enthalpy difference of the reactions leading to equation (12) were reported to vary substantially depending on the pH, ionic strength, and metabolite concentration in the cell. When one mole of glucose synthesizes 30 moles of ATP, the measured heat release varies between 879 to 4017 kJ for each mole of consumed glucose. Comparison of the theoretical first and the second law efficiencies of the muscle work production with the experimental measurements are given in Table 3, when we compare the theoretical maximum limits with the literature values given in Table 4; the measured first law efficiencies appear dramatically lower. One of the reasons for this observation is the reference to the "*muscle elongation work"*, which is defined as the product of the force and the displacement as "*work*", without accounting for all the other types of work that a cell has to perform, such as pumping ions from a low concentration zone to a high concentration zone, synthesizing enzymes etc., which is only a fraction of the total work done by the cell. This situation is evidenced by Han *et al* (2013), who reported that 35% greater maximum mechanical efficiency of the right ventricular muscle is offset by the greater metabolic cost of activation of the left ventricular trabeculae, when work is calculated in terms of the shortening velocity and power. Different experimental protocols and temperatures are used in most of the previous studies; exclusion of the energy expenditure for pumping the ions from the efficiency calculations is usually achieved on purpose during the design of the experiments (Barclay and Weber 2004). Among the factors complicating the experimental measurements, we may account the fraction of the energy, which may be stored in the elastic connections between the myofibrils (Linari *et al* 2003); and the energy which is absorbed during lengthening of the muscle, and converted into mechanical work during subsequent shortening (Constable *et al* 1997).

The muscle work efficiencies listed in Table 3 are subject to variance and may change even in the different muscles of the same organism depending on their biological properties: Han *et al* (2013) reported 35% greater maximum mechanical efficiency of the rat right ventricular muscle than that of the left ventricular trabeculae. The muscle work efficiency may vary with time even in the same muscle: Barclay and Weber (2004) after determining the work output and heat production in *in vitro* experiments with the slow-twitch soleus and fast-twitch extensor digitorum longus muscle fibers from mouse reported that during the first second of the experiments the efficiency was greater in the slow-twitch soleus muscle, than it was in the fast-twitch extensor digitorum longus muscle, but there was no difference in the net efficiency of the muscles in the longer time span. Yaniv *et al* (2013) argue that the myocardial ATP supply and demand mechanisms are age dependent. Although very large numbers of papers are available in the literature, the complexity of the topic implies that there is still need for more research to understand the details in the cellular systems, which are not studied in detail yet. Moreover, mammalian skeletal muscle fibers distinguished by contents of phosphocreatine, ATP, and P_i, making the topic even more complicated (Kushmerick et al 1992). Therefore the estimates of the maximum energy and the exergy efficiencies of this process are very important, since they are invariable fixed numbers, and the deviation from these maximum efficiencies, beyond an acceptable range, may actually point a health problem.

Conclusion

An analogy between the Carnot engine and muscle is developed to gain insight about the muscle work production process and to estimate the highest attainable thermodynamic

efficiency for the nutrients-energy to muscle-work conversion. The measured first law muscle work efficiencies obtained from the literature are lower than the maximum theoretical first law efficiency. One of the reasons for this is the definition of the muscle elongation work in the literature as the product of the force and the displacement, which excludes the additional work that a cell has to perform, such as pumping ions from a low concentration zone to a high concentration zone, synthesizing enzymes etc.

The results of the previous research concerning thermic effect of the foods are not consistent (Granata and Brandon, 2002). Our study offers a partial solution to this situation by offering an estimate of the maximum heat which may be released from a muscle.

The most important consequence of this study is the determination of the maximum attainable values of the energy and exergy efficiency of the muscle work, a deviation from these values, especially if it reaches unacceptable levels, may indicate a serious health problem.

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Table 1. Analogous components of the Carnot heat engine and the ideal muscle

Carnot Engine	**Ideal Muscle**
High temperature reservoir at T_{high}	Arteries containing high concentrations of nutrients (e.g. glucose, fatty acids etc.) and O_2
Low temperature reservoir at T_{low}	Veins containing low concentrations of nutrients (e.g. glucose, fatty acids etc.) and O_2
Heat input (Q_{high})	Total Gibbs free energy entering the cell with nutrients $\sum n_{in}(h - Ts)_{in}$

	Where n_{in}: number of the moles of nutrients entering into the cell, h: enthalpy/mole of nutrients, s: entropy/mole of nutrients, T: temperature of the nutrients
Waste heat (Q_{low})	Total Gibbs free energy exiting the cell with the catabolic waste (i.e. CO_2 and H_2O) $\sum n_{out}(h-Ts)_{out}$ where n_{out}: number of the moles of waste leaving the cell, h: enthalpy/mole of waste, s: entropy/mole of waste, T: temperature of the waste stream
Temperature (T)	Chemical potential (μ)

Table 2. Enthalpy and Gibbs free energy of formation of the metabolites involved in Reaction (13) at 310.15 K, pH=7, I=0.18

	Glucose	*Oxygen*	*Water*	*Carbon dioxide*
$\Delta H^T_{f,i}$ (kJ/mol)	*-1267*	*-12*	*-287*	*-701*
$\Delta G^T_{f,i}$ (kJ/mol)	*2080*	*22*	*-149*	*-127*

Table 3. The first and second law efficiencies of the muscle work production

	Theoretical limits		Experimental data	
	reversible process (maximum work production)	no work done (maximum heat production)	minimum heat release (Smith et al., 2008)	maximum heat release (Smith et al., 2008)
X_{loss}	0	0	-	-
W (kJ/mol glucose)	3862	0	3707	569
Q (kJ/mol glucose)	724	4586	879	4017
η_I	0.84	0	0.81	0.12
η_{II}	1	0	0.96	0.14

Table 4. First and second law efficiencies of isolated muscles undergoing full contraction cycles. First law efficiencies, η_I, are taken from Smith *et al* (2008) which present the averages values reported by Gibbs and Chapman (1974), Heglund and Cavagna (1987), and Barclay (1996). The second law efficiencies, η_{II}, are calculated with ΔH=-4586 kJ/mol of glucose and ΔG=-3862 kJ/mol of glucose (Genç et al., 2013a).

Muscle	*T(°C)*	η_I	η_{II}
Tortoise rectus femoris	*15*	*0.35*	*0.42*
Frog sartorius	*12*	*0.25*	*0.30*
Rat soleus	*20*	*0.17*	*0.20*
Mouse soleus	*35*	*0.15*	*0.18*
Mouse EDL	*35*	*0.14*	*0.17*

Figure Captions

Fig. 1. Schematic diagram of the Carnot engine

Fig. 2. Schematic diagram of the ideal muscle

Fig. 3. Exergy flow diagram in the ideal muscle. The ideal muscle system is represented as two sub-systems: cell and ATP-sink. Cell represents the cellular energy metabolism, where nutrients are catabolized and ATP is produced. ATP-sink represents the consumption of ATP and the muscle contraction, where work is produced.

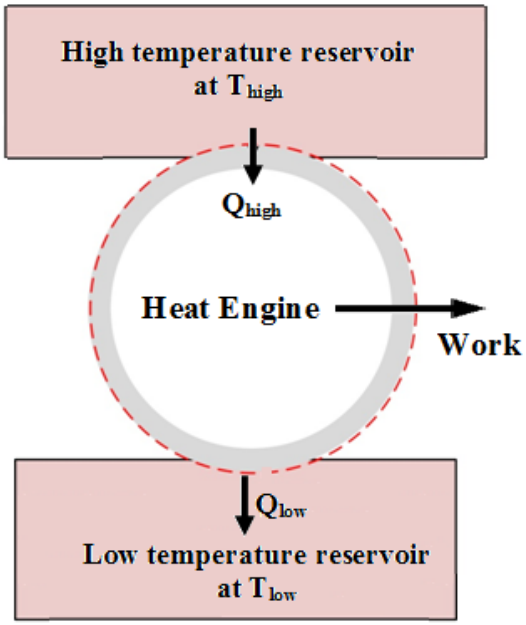
High temperature reservoir
at T_{high}
Q_{high}
Heat Engine
Work
Q_{low}
Low temperature reservoir
at T_{low}

Fig. 1

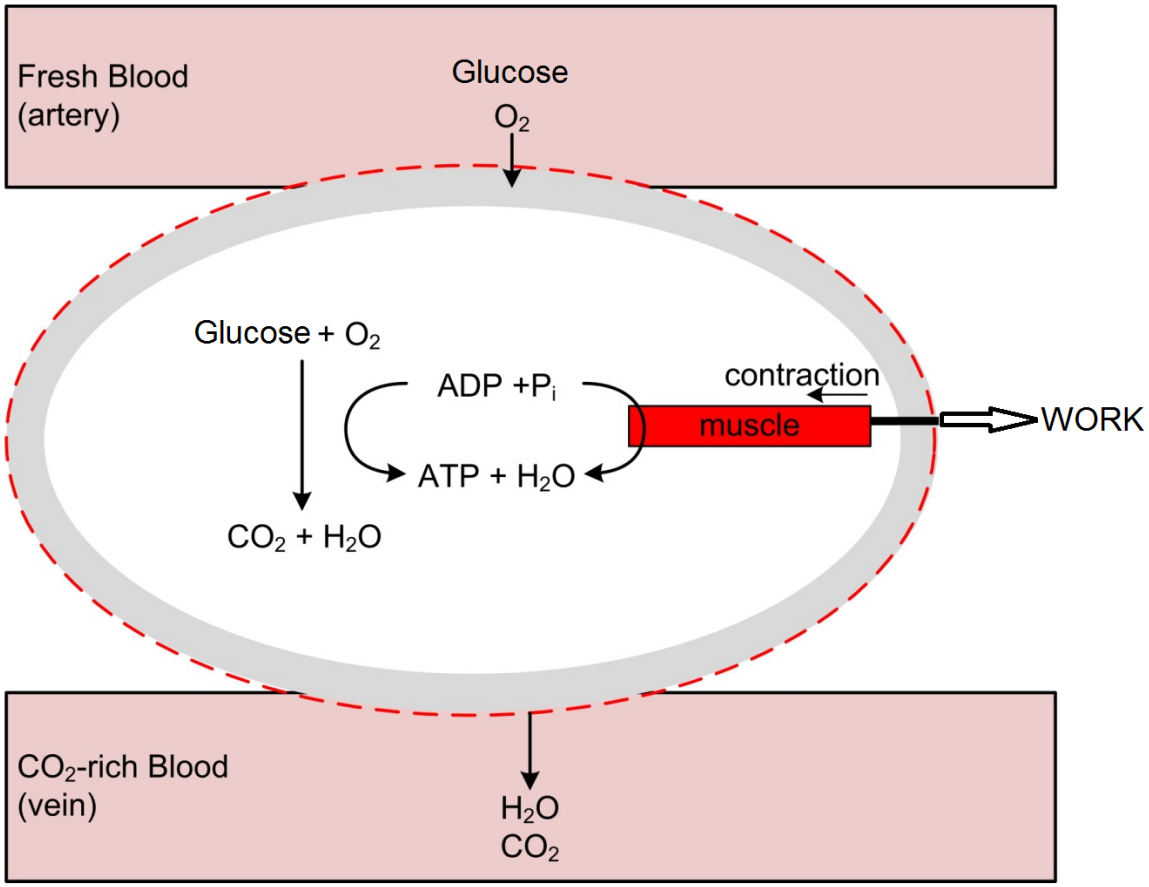
Fresh Blood
(artery)
Glucose
O_2
Glucose + O_2
ADP +P_i
contraction
muscle
WORK
ATP + H_2O
CO_2 + H_2O
CO_2-rich Blood
(vein)
H_2O
CO_2

Fig. 2

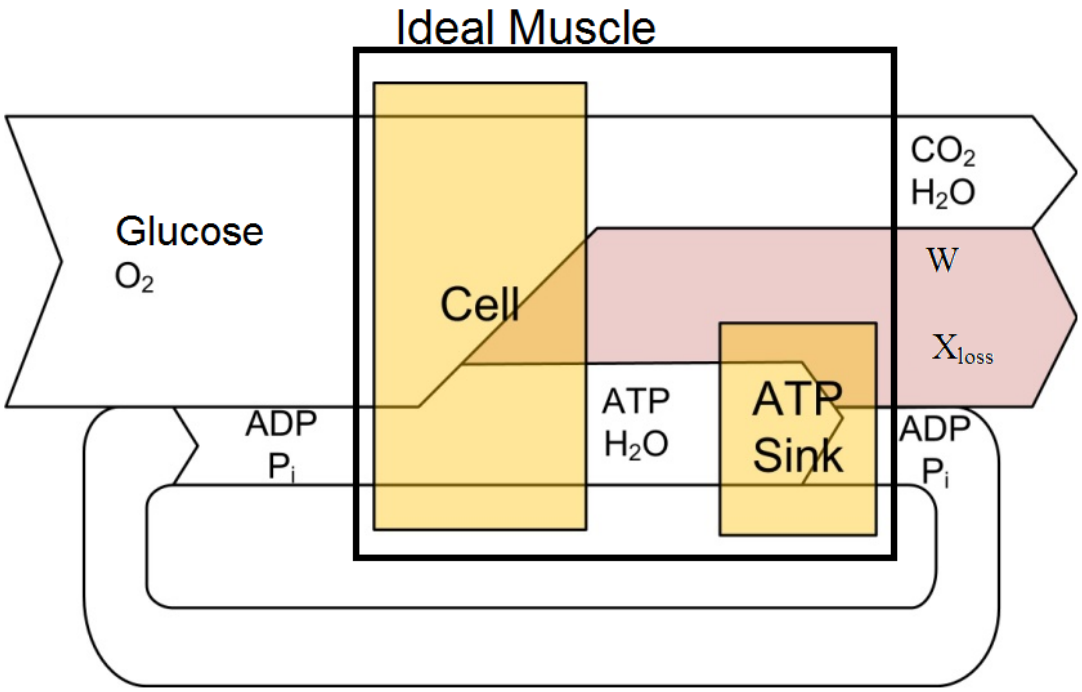
Ideal Muscle
Glucose
O_2
Cell
CO_2
H_2O
W
X_{loss}
ATP
H_2O
ATP
Sink
ADP
P_i
ADP
P_i

Fig. 3.